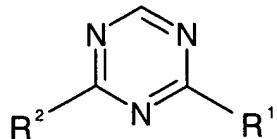


B1
--35. A method of treating polycystic kidney disease comprising administration of a composition comprising an effective amount of a compound of any of claims 1-7 and 10-21.--

Amend Claims 1, 6, 22 and 24-27 as follows:

1. A compound having the formula:



wherein,

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Each R¹ and R² is independently R³; R⁸; NHR³; NHR⁵; NHR⁶; NR⁵R⁵; NR⁵R⁶; heterocyclyl optionally substituted with 1-4 independent R⁴ on each ring; or C1-C10 alkyl substituted with 1-4 independent R⁴;

Each R³ is independently aryl; phenyl optionally substituted with 1-5 independent R⁴ on each ring; or heteroaryl optionally substituted with 1-4 independent R⁴ on each ring;

Each n is independently 1 or 2;

Each m is independently 0, 1, 2, 3, or 4;

Each R⁴ is independently selected from H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R⁸; halo; haloalkyl; SR⁵; OR⁵; OC(O)R⁵; NR⁵R⁵; NR⁵R⁶; NR⁵R¹⁶; COOR⁵; NO₂; CN; C(O)R⁵; C(O)C(O)R⁵; C(O)NR⁵R⁵; S(O)_nR⁵; S(O)_nNR⁵R⁵; NR⁵C(O)NR⁵R⁵; NR⁵C(O)C(O)R⁵; NR⁵C(O)R⁵; NR⁵(COOR⁵); NR⁵C(O)R⁸; NR⁵S(O)_nNR⁵R⁵; NR⁵S(O)_nR⁵; NR⁵S(O)_nR⁸; NR⁵C(O)C(O)NR⁵R⁵; NR⁵C(O)C(O)NR⁵R⁶; OC(O)NR⁵R⁵; OS(O)_nNR⁵R⁵; NR⁵S(O)_nOR⁵; P(O)(OR⁵)₂; C1-C10 alkyl substituted with 1-3 independent aryl, R⁷ or R⁸; or C2-C10 alkenyl substituted with 1-3 independent aryl, R⁷ or R⁸;

Each R⁵ is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R⁹; haloalkyl; C1-C10 alkyl substituted with 1-3 independent aryl, R⁷ or R⁹ groups; C3-C10 cycloalkyl substituted with 1-3 independent aryl, R⁷ or R⁹ groups; or C2-C10 alkenyl substituted with 1-3 independent aryl, R⁷ or R⁹;

Each R⁶ is independently C(O)R⁵, COOR⁵, C(O)NR⁵R⁵, C(=N R⁵) NR⁵R⁵, or S(O)_n R⁵;

Each R⁷ is independently halo, CF₃, SR¹⁰, OR¹⁰, OC(O)R¹⁰, NR¹⁰R¹⁰, NR¹⁰R¹¹, NR¹¹R¹¹, COOR¹⁰, NO₂, CN, C(O)R¹⁰, OC(O)NR¹⁰R¹⁰, C(O)NR¹⁰R¹⁰, N(R¹⁰)C(O)R¹⁰, N(R¹⁰) (COOR¹⁰), S(O)_nNR¹⁰R¹⁰; NR¹⁰S(O)_nNR¹⁰R¹⁰; NR¹⁰S(O)_nR¹⁰; or P(O)(OR⁵)₂;

Each R⁸ is independently a 3-8 membered monocyclic, 7-12 membered bicyclic, or 11-14 membered tricyclic ring system having 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms independently selected from O, N, or S, which may be saturated or unsaturated, and wherein 0, 1, 2, 3 or 4 atoms of each ring may be substituted by a substituent independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R⁹; halo; sulfur; oxygen; CF₃; SR⁵; OR⁵; OC(O)R⁵; NR⁵R⁶; NR⁶R⁶; COOR⁵; NO₂; CN; C(O)R⁵; C(O)NR⁵R⁵; S(O)_nNR⁵R⁵; NR⁵C(O)NR⁵R⁵; NR⁵C(O)R⁹; NR⁵S(O)_nNR⁵R⁵; NR⁵S(O)_nR⁹; C1-C10 alkyl substituted with 1-3 independent R⁷, R⁹ or aryl; or C2-C10 alkenyl substituted with 1-3 independent R⁷, R⁹ or aryl;

Each R⁹ is independently a 3-8 membered monocyclic, 7-12 membered bicyclic, or 11-14 membered tricyclic ring system having 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms independently selected from O, N, or S, which may be saturated or unsaturated, and wherein 0, 1, 2 or 3 atoms of each ring may be substituted by a substituent independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; halo; sulfur; oxygen; CF₃; haloalkyl; SR¹⁰; OR¹⁰; NR¹⁰R¹⁰; NR¹⁰R¹¹; NR¹¹R¹¹; COOR¹⁰; NO₂; CN; C(O)R¹⁰; S(O)_nR¹⁰; S(O)_nNR¹⁰R¹⁰; or C(O)NR¹⁰R¹⁰;

Each R¹⁰ is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; haloalkyl; C1-C10 alkyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, OR¹², SR¹², NR¹²R¹², COOR¹², NO₂, CN, C(O)R¹², C(O)NR¹²R¹², NR¹²C(O)R¹², N(R¹²)(COOR¹²), S(O)_nNR¹²R¹², or OC(O)R¹²; or phenyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF₃, OR¹², SR¹², NR¹²R¹², COOR¹², NO₂, CN, C(O)R¹², C(O)NR¹²R¹², NR¹²C(O)R¹², N(R¹²)(COOR¹²), S(O)_nNR¹²R¹², or OC(O)R¹²;

Each R¹¹ is independently C(O)R¹⁰, COOR¹⁰, C(O)NR¹⁰R¹⁰ or S(O)_nR¹⁰;

Each R¹² is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; C1-C10 alkyl substituted with 1-3 independent C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF₃, OR¹³, SR¹³, NR¹³R¹³, COOR¹³, NO₂, CN, C(O)R¹³, C(O)NR¹³R¹³, NR¹³C(O)R¹³, or OC(O)R¹³; or phenyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF₃, OR¹³, SR¹³, NR¹³R¹³, COOR¹³, NO₂, CN, C(O)R¹³, C(O)NR¹³R¹³, NR¹³C(O)R¹³, or OC(O)R¹³;

Each R¹³ is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; C1-C10 alkyl optionally substituted with halo, OR¹⁴, SR¹⁴, NR¹⁴R¹⁴, COOR¹⁴, NO₂, CN; or phenyl optionally substituted with halo, CF₃, OR¹⁴, SR¹⁴, NR¹⁴R¹⁴, COOR¹⁴, NO₂, CN;

Each R¹⁴ is independently H; C1-C10 alkyl; C3-C10 cycloalkyl or phenyl;

Each R¹⁶ is independently H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R⁸; halo; haloalkyl; COOR⁵; C(O)R⁵; C(O)C(O)R⁵; C(O)NR⁵R⁵; S(O)_nR⁵; S(O)_nNR⁵R⁵; C1-C10 alkyl substituted with 1-3 independent aryl, R⁷, R⁸, or phenyl optionally substituted with substituted with 1-4 independent R²³; or C2-C10 alkenyl substituted with 1-3 independent aryl, R⁷ or R⁸;

Each R²³ is independently selected from H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R⁸; halo; haloalkyl; SR⁵; OR⁵; OC(O)R⁵; NR⁵R⁵; NR⁵R⁶; COOR⁵; NO₂; CN; C(O)R⁵; C(O)C(O)R⁵; C(O)NR⁵R⁵; S(O)_nR⁵; S(O)_nNR⁵R⁵; NR⁵C(O)NR⁵R⁵; NR⁵C(O)C(O)R⁵; NR⁵C(O)R⁵; NR⁵(COOR⁵); NR⁵C(O)R⁸; NR⁵S(O)_nNR⁵R⁵; NR⁵S(O)_nR⁵; NR⁵S(O)_nR⁸; NR⁵C(O)C(O)NR⁵R⁵; NR⁵C(O)C(O)NR⁵R⁶; OC(O)NR⁵R⁵; OS(O)_nNR⁵R⁵; NR⁵S(O)_nOR⁵; P(O)(OR⁵)₂; C1-C10 alkyl substituted with 1-3 independent aryl, R⁷ or R⁸; or C2-C10 alkenyl substituted with 1-3 independent aryl, R⁷ or R⁸;

Each haloalkyl is independently a C1-C10 alkyl substituted with one or more halogen atoms, selected from F, Cl, Br, or I, including perhaloalkyl;

Each aryl is independently a 6-carbon monocyclic, 10-carbon bicyclic or 14-carbon tricyclic aromatic ring system optionally substituted with 1-3 independent C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; R⁹; halo; haloalkyl; OR¹⁰; SR¹⁰; NR¹⁰R¹⁰; NR¹⁰R¹¹; COOR¹⁰; NO₂; CN; C(O)R¹⁰; C(O)C(O)R¹⁰; C(O)NR¹⁰R¹⁰; N(R¹⁰)C(O)NR¹⁰R¹⁰; N(R¹⁰)C(O)R¹⁰; N(R¹⁰)S(O)_nR¹⁰; N(R¹⁰)(COOR¹⁰); NR¹⁰C(O)C(O)R¹⁰;

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$\text{NR}^{10}\text{C(O)R}^9$; $\text{NR}^{10}\text{S(O)}_n\text{NR}^{10}\text{R}^{10}$; $\text{NR}^{10}\text{S(O)}_n\text{R}^9$; $\text{NR}^{12}\text{C(O)C(O)NR}^{12}\text{R}^{12}$; $\text{S(O)}_n\text{R}^{10}$; $\text{S(O)}_n\text{NR}^{10}\text{R}^{10}$; OC(O)R^{10} ; C1-C10 alkyl substituted with 1-3 independent R^9 , halo, CF_3 , OR^{10} , SR^{10} , OC(O)R^{10} , $\text{NR}^{11}\text{R}^{11}$, $\text{NR}^{10}\text{R}^{10}$, $\text{NR}^{10}\text{R}^{11}$, COOR^{10} , NO_2 , CN, C(O)R^{10} , $\text{OC(O)NR}^{10}\text{R}^{10}$, $\text{C(O)NR}^{10}\text{R}^{10}$, $\text{N(R}^{10})\text{C(O)R}^{10}$, $\text{N(R}^{10})(\text{COOR}^{10})$, $\text{S(O)}_n\text{NR}^{10}\text{R}^{10}$; R^{10} ; or C2-C10 alkenyl substituted with 1-3 independent R^9 , halo, CF_3 , OR^{10} , SR^{10} , OC(O)R^{10} , $\text{NR}^{11}\text{R}^{11}$, $\text{NR}^{10}\text{R}^{10}$, $\text{NR}^{10}\text{R}^{11}$, COOR^{10} , NO_2 , CN, C(O)R^{10} , $\text{OC(O)NR}^{10}\text{R}^{10}$, $\text{C(O)NR}^{10}\text{R}^{10}$, $\text{N(R}^{10})\text{C(O)R}^{10}$, $\text{N(R}^{10})(\text{COOR}^{10})$, $\text{S(O)}_n\text{NR}^{10}\text{R}^{10}$;

Each heterocyclyl is independently a 3-8 membered nonaromatic monocyclic, 8-12 membered nonaromatic bicyclic, or 11-14 membered nonaromatic tricyclic, ring system having 1-4 heteroatoms if monocyclic, 1-8 heteroatoms if bicyclic, or 1-10 heteroatoms if tricyclic, said heteroatoms independently selected from O, N, or S;

Each heteroaryl is independently a 5-8 membered aromatic monocyclic, 8-12 membered aromatic bicyclic, or 11-14 membered aromatic tricyclic ring system having 1-4 heteroatoms if monocyclic, 1-8 heteroatoms if bicyclic, or 1-10 heteroatoms if tricyclic, said heteroatoms independently selected from O, N, or S;

provided R^1 and R^2 are not both 1-alkylpyridinium, or both 4-pyridyl;

further provided neither R^1 or R^2 is morpholino or NH_2 ;

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6. The compound of claim 1 wherein,

R^1 is independently NHR^5 ;

R^2 is independently NHR^3 ;

Each R^3 is independently aryl; phenyl optionally substituted with 1-5 independent R^4 on each ring; or heteroaryl optionally substituted with 1-4 independent R^4 on each ring;

Each R^4 is independently selected from H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^8 ; halo; CF_3 ; SR^5 ; OR^5 ; OC(O)R^5 ; NR^5R^5 ; NR^5R^6 ; NR^5R^{16} ; COOR^5 ; NO_2 ; CN; C(O)R^5 ; C(O)C(O)R^5 ; $\text{C(O)NR}^5\text{R}^5$; $\text{S(O)}_n\text{R}^5$; $\text{S(O)}_n\text{NR}^5\text{R}^5$; $\text{NR}^5\text{C(O)NR}^5\text{R}^5$; $\text{NR}^5\text{C(O)C(O)R}^5$; $\text{NR}^5\text{C(O)R}^5$; $\text{NR}^5(\text{COOR}^5)$; $\text{NR}^5\text{C(O)R}^8$; $\text{NR}^5\text{S(O)}_n\text{NR}^5\text{R}^5$; $\text{NR}^5\text{S(O)}_n\text{R}^5$; $\text{NR}^5\text{S(O)}_n\text{R}^8$; $\text{NR}^5\text{C(O)C(O)NR}^5\text{R}^5$; $\text{NR}^5\text{C(O)C(O)NR}^5\text{R}^6$; $\text{OC(O)NR}^5\text{R}^5$; $\text{OS(O)}_n\text{NR}^5\text{R}^5$; $\text{NR}^5\text{S(O)}_n\text{OR}^5$; $\text{P(O)(OR}^5)_2$; C1-C10 alkyl substituted with 1-3 independent aryl, R^7 or R^8 ; or C2-C10 alkenyl substituted with 1-3 independent aryl, R^7 or R^8 ;

Each R⁵ is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R⁹; haloalkyl; C1-C10 alkyl substituted with 1-3 independent aryl, R⁷ or R⁹ groups; C3-C10 cycloalkyl substituted with 1-3 independent aryl, R⁷ or R⁹ groups; or C2-C10 alkenyl substituted with 1-3 independent aryl, R⁷ or R⁹;

Each R⁶ is independently C(O)R⁵, COOR⁵, C(O)NR⁵R⁵, C(=NR⁵)NR⁵R⁵, or S(O)_nR⁵;

Each R⁷ is independently halo, CF₃, SR¹⁰, OR¹⁰, OC(O)R¹⁰, NR¹⁰R¹⁰, NR¹⁰R¹¹, NR¹¹R¹¹, COOR¹⁰, NO₂, CN, C(O)R¹⁰, OC(O)NR¹⁰R¹⁰, C(O)NR¹⁰R¹⁰, N(R¹⁰)C(O)R¹⁰, N(R¹⁰)(COOR¹⁰), S(O)_nNR¹⁰R¹⁰; NR¹⁰S(O)_nNR¹⁰R¹⁰; NR¹⁰S(O)_nR¹⁰; or P(O)(OR⁵)₂;

Each R⁸ is independently a 3-8 membered monocyclic, 7-12 membered bicyclic, or 11-14 membered tricyclic ring system having 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms independently selected from O, N, or S, which may be saturated or unsaturated, and wherein 0, 1, 2, 3 or 4 atoms of each ring may be substituted by a substituent independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R⁹; halo; sulfur; oxygen; CF₃; SR⁵; OR⁵; OC(O)R⁵; NR⁵R⁵; NR⁵R⁶; NR⁶R⁶; COOR⁵; NO₂; CN; C(O)R⁵; C(O)NR⁵R⁵; S(O)_nNR⁵R⁵; NR⁵C(O)NR⁵R⁵; NR⁵C(O)R⁹; NR⁵S(O)_nNR⁵R⁵; NR⁵S(O)_nR⁹; C1-C10 alkyl substituted with 1-3 independent R⁷, R⁹ or aryl; or C2-C10 alkenyl substituted with 1-3 independent R⁷, R⁹ or aryl;

Each R⁹ is independently a 3-8 membered monocyclic, 7-12 membered bicyclic, or 11-14 membered tricyclic ring system having 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms independently selected from O, N, or S, which may be saturated or unsaturated, and wherein 0, 1, 2 or 3 atoms of each ring may be substituted by a substituent independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; halo; sulfur; oxygen; CF₃; haloalkyl; SR¹⁰; OR¹⁰; NR¹⁰R¹⁰; NR¹⁰R¹¹; NR¹¹R¹¹; COOR¹⁰; NO₂; CN; C(O)R¹⁰; S(O)_nR¹⁰; S(O)_nNR¹⁰R¹⁰; or C(O)NR¹⁰R¹⁰;

Each R¹⁰ is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; haloalkyl; C1-C10 alkyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, OR¹², SR¹², NR¹²R¹², COOR¹², NO₂, CN, C(O)R¹², C(O)NR¹²R¹², NR¹²C(O)R¹², N(R¹²)(COOR¹²), S(O)_nNR¹²R¹², or OC(O)R¹²; or phenyl optionally substituted with 1-3

independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF₃, OR¹², SR¹², NR¹²R¹², COOR¹², NO₂, CN, C(O)R¹², C(O)NR¹²R¹², NR¹²C(O)R¹², N(R¹²)(COOR¹²), S(O)_nNR¹²R¹², or OC(O)R¹²;

Each R¹¹ is independently C(O)R¹⁰, COOR¹⁰, C(O)NR¹⁰R¹⁰ or S(O)_nR¹⁰;

Each R¹² is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; C1-C10 alkyl substituted with 1-3 independent C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF₃, OR¹³, SR¹³, NR¹³R¹³, COOR¹³, NO₂, CN, C(O)R¹³, C(O)NR¹³R¹³, NR¹³C(O)R¹³, or OC(O)R¹³; or phenyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF₃, OR¹³, SR¹³, NR¹³R¹³, COOR¹³, NO₂, CN, C(O)R¹³, C(O)NR¹³R¹³, NR¹³C(O)R¹³, or OC(O)R¹³;

Each R¹³ is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; C1-C10 alkyl optionally substituted with halo, OR¹⁴, SR¹⁴, NR¹⁴R¹⁴, COOR¹⁴, NO₂, CN; or phenyl optionally substituted with halo, CF₃, OR¹⁴, SR¹⁴, NR¹⁴R¹⁴, COOR¹⁴, NO₂, CN;

Each R¹⁴ is independently H; C1-C10 alkyl; C3-C10 cycloalkyl or phenyl;

Each R¹⁶ is independently H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R⁸; halo; CF₃; COOR⁵; C(O)R⁵; C(O)C(O)R⁵; C(O)NR⁵R⁵; S(O)_nNR⁵R⁵; C1-C10 alkyl substituted with 1-3 independent aryl, R⁷, R⁸, or phenyl optionally substituted with substituted with 1-4 independent R²³; or C2-C10 alkenyl substituted with 1-3 independent aryl, R⁷ or R⁸; and

Each R²³ is independently selected from H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R⁸; halo; CF₃; SR⁵; OR⁵; OC(O)R⁵; NR⁵R⁶; COOR⁵; NO₂; CN; C(O)R⁵; C(O)C(O)R⁵; C(O)NR⁵R⁵; S(O)_nNR⁵R⁵; NR⁵C(O)NR⁵R⁵; NR⁵C(O)C(O)R⁵; NR⁵C(O)R⁵; NR⁵(COOR⁵); NR⁵C(O)R⁸; NR⁵S(O)_nNR⁵R⁵; NR⁵S(O)_nR⁵; NR⁵S(O)_nR⁸; NR⁵C(O)C(O)NR⁵R⁵; NR⁵C(O)C(O)NR⁵R⁶; OC(O)NR⁵R⁵; OS(O)_nNR⁵R⁵; NR⁵S(O)_nOR⁵; P(O)(OR⁵)₂; C1-C10 alkyl substituted with 1-3 independent aryl, R⁷ or R⁸; or C2-C10 alkenyl substituted with 1-3 independent aryl, R⁷ or R⁸;

provided neither R¹ nor R² is NH₂.

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22. A composition comprising a compound of any of claims 1-7 and 10-21 and a pharmaceutically acceptable carrier.

24. A method of treating kinase-mediated disease or disease symptoms in a mammal comprising administration of a composition comprising an effective amount of a compound of any of claims 1-7 and 10-21.

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25. A method of inhibiting kinase activity in a mammal comprising administration of a composition comprising an effective amount of a compound of any of claims 1-7 and 10-21.

26. A method of treating disease or disease symptoms in a mammal comprising administration of a composition comprising an effective amount of a compound of any of claims 1-7 and 10-21.

27. A method of inhibiting angiogenesis or vasculogenesis activity in a mammal comprising administration of a composition comprising an effective amount of a compound of any of claims 1-7 and 10-21.